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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/057,629	01/25/2002	Harry R. Davis	CV01382K	2175

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PATENT DEPARTMENT (K-6-1, 1990)
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EXAMINER	
HUI, SAN MING R	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 02/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/057,629	DAVIS, HARRY R.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47 and 53-58* is/are pending in the application.

4a) Of the above claim(s) *2-7,12,25-31,46,47,57 and 58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,8-11,13-24,32-45 and 53-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments filed November 17, 2004 have been entered.

Claims 25-31, 46-47, and 57-58 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in response filed August 4, 2003.

Claims 2-7, and 12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in response filed August 4, 2003.

Claims 1, 8-11, 13-24, 32-45, and 53-56 have been examined herein to the extent they read on the elected invention and species.

The outstanding rejection under 35 USC 112, second paragraph is withdrawn in view of the amendments filed November 17, 2004.

Applicant's remarks with regard to claim 56 have been considered and are found persuasive to withdraw the rejections under 35 USC 102.

Examiner apologizes the overlook in the numbering of claims rejected in 35 USC 103(a) set forth in the previous office action mailed October 20, 2004. Claim 56 should also be rejected under 35 USC 103 along with the other claims rejected therein since

the rejection set forth in the previous office action and the cited prior art did address the combination of the herein claimed actives with a bile sequestrant.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 8-9, 10-11, 13-24, 32-45, and 53-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over '966 in view of Belamarich et al. (Pediatrics, 1990;86(6):977-981).

'966 also teaches the elected compound herein, ezetimibe, with HMG-CoA reductase inhibitors such as simvastatin, useful for reducing cholesterol and the risk of artherosclerosis (See the abstract, also col. 32, Example 6, Compound 6A, and col. 40, line 52 particularly, claims 6 and 10). '966 also teaches the dosage of ezetimibe for treating hypercholesterolemia as0.1-30 or 0.1-15 mg/kg (see col. 21, line 17-19). '966

also teaches the dosage of HMG-CoA reductase inhibitors as 10-80mg daily to 1-1000mg daily depending upon the agents used (See col. 21, lines 27-42).

'966 does not expressly teach the employing of ezetimibe with simvastatin, a HMG-CoA reductase inhibitor and/or cholestyramine, in the dosage herein claimed to treat sitosterolemia.

Belamarich et al. teaches that hypercholesterolemia is one of the manifestation of sitosterolemia (See page 977, col. 2, second to last paragraph). Belamarich et al. also teaches cholestyramine and low-sterol diet as effective in lowering the both cholesterol and sterol levels in sitosterolemic pateints (See page 979, col. 2, last paragraph bridging page 980, col. 1, first full paragraph).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ ezetimibe with simvastatin and/or cholestyramine, in the dosage herein claimed to treat sitosterolemia.

One of ordinary skill in the art would have been motivated to employ ezetimibe with simvastatin and/or cholestyramine, in the dosage herein claimed to treat sitosterolemia. '966 teaches the combination of simvastatin and ezetimibe as useful in reducing cholesterol level. Employing the combination of simvastatin and ezetimibe in a method to reduce cholesterol level and thereby treating sitosterolemia, a condition known to have elevated cholesterol level, would have been reasonably expected to be effective, absent evidence to the contrary. Moreover, cholestyramine is known to be effective in lowering cholesterol in sitosterolemic patient. Therefore, administering all three compounds concomitantly for the very same purpose would have been obvious to

one of ordinary skill in the art (See *In re Kerkhoven* 205 USPQ 1069). Furthermore, optimization of result effect parameters (e.g., dosage range, dosing regimens) is obvious as being within the skill of the artisan.

Response to Arguments

Applicant's arguments filed November 17, 2004 averring compounds useful to treat hypercholesterolemia not necessarily effective in treating sitosterolemia have been fully considered but they are not persuasive. Attention is directed to Hidaka et al. (reference of record), Hidaka et al. teaches a HMG-CoA reductase in hibitor as effective in treating sitosterolemia that it can reduce the plant sterol level in sitosterolemic patients. Therefore, employing HMG-CoA reductase inhibitor in a method of treating sitosterolemia along with other agents such as those herein claimed would be reasonably expected to be successful and effective.

Applicant's arguments with regard to long felt need have been considered, but are not found persuasive. Applicant argues that the claimed subject matter solved a problem that was long standing in the art. However, there is no showing that others of ordinary skill in the art were working on the problem and if so, for how long. In addition, there is no evidence that if persons skilled in the art who were presumably working on the problem knew of the teachings of the above cited references, they would still be unable to solve the problem. See MPEP § 716.04.

Applicant's arguments filed November 17, 2004 averring certain type of sitosterolemic patients having normal cholesterol level have been considered, but are

not found persuasive. The arguments are drawn to unclaimed limitation since the instant claims do not exclude any types of sitosterolemic patients.

Applicant's arguments field November 17, 2004 averring teaching away by Belamarich have been considered, but are not found persuasive since HMG-CoA reductase inhibitors, such as pravastatin, was shown to be effective when using in combination with cholestyramine to treat sitosterolemia.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax

phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

San-ming Hui
Primary Examiner
Art Unit 1617